

Synthesis of Multi-core–shell Magnetic Molecularly Imprinted Microspheres for Rapid Recognition of Dicofol in Tea

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ABSTRACT: Magnetic multi-core–shell molecularly imprinted microspheres ($\text{Fe}_3\text{O}_4\text{@MIMs}$) based on multi- Fe_3O_4 nanoparticles as core structures and dummy imprinted materials as shell structures have been synthesized by a surface-imprinted technique using dichlorodiphenyltrichloroethane as the dummy template and were successfully used as a specific adsorbent for rapid isolation of trace levels of dicofol from teas. The resulting $\text{Fe}_3\text{O}_4\text{@MIMs}$ were characterized by scanning electron microscopy, Fourier transform infrared spectroscopy, X-ray diffraction, vibrating sample magnetometer, and thermogravimetric analysis. In comparison to the imprinted polymers prepared by the traditional polymerizations, the obtained $\text{Fe}_3\text{O}_4\text{@MIMs}$ showed regularly spherical shape, porous morphologies, high saturation magnetization [56.8 electromagnetic units (emu)/g], and rapid response time (15 s). The as-synthesized $\text{Fe}_3\text{O}_4\text{@MIMs}$, which incorporated the excellent molecular recognition and magnetic separation properties, were successfully used as special adsorbents for rapid isolation and extraction of trace levels of dicofol and its analogues from a complicated tea matrix.

KEYWORDS: Multi-core–shell imprinted microsphere, magnetic separation, rapid isolation and extraction, dicofol, tea

INTRODUCTION

Molecular imprinting technology is attracting widespread attention because of its potential to deliver robust molecular recognition elements targeted toward essentially any guest present in various environments.¹ Molecularly imprinted microspheres (MIMs) can be readily tailored with special selectivity for a guest molecule, which is accomplished by synthesizing a network imprinted polymer in the presence of a template molecule.^{2–5} When the template molecule is removed, a highly specific microcavity will be formed within the rigid three-dimensional polymer matrix, which has a high binding affinity toward the template molecule.^{6–9} The MIMs possess several advantages over their biological counterparts, including low-cost, simple, and convenient preparation, storage stability, repeated operations without the loss of activity, high mechanical strength, durability to heat and pressure, and applicability in harsh chemical media.^{10–12} However, MIMs suffer from some drawbacks in their practical applications. For example, the small particle sizes bring difficulties when trying to separate them from aqueous samples, which eventually prevent them from real application.¹³

Recently, magnetic materials have been considered ideal candidates for the biological and environmental applications, because they have unique magnetic properties to be handled by the magnetic field and allow for the separation of the target from the samples.^{14,15} Magnetic materials are commonly synthesized on the basis of spherical or particle shape magnetic cores, which are further modified with a suitable material on the surface to form various configurations, such as core–shell structures.^{16–18} As known, the magnetic materials as adsorbents have several advantages in comparison to other traditional adsorbents. The separation process can be performed directly in the sample solution containing the magnetic adsorbent, and the magnetic particles can be simply collected and separated

from the liquid phase under a magnetic field, which avoids the tedious filtration or centrifugation procedure.¹⁹

Combining the molecular imprinting technique with magnetic polymer beads will provide a new approach toward separation application and broaden the use of MIMs. Therefore, when magnetic materials are coated with thin imprinted polymers, these suspended materials not only provide the selectivity for the target molecules but also have the ability of one-step separation by a magnet.^{20,21} Moreover, the structure of the magnetic supporter (multi-cores), rather than a single Fe_3O_4 particle as reported in the previous studies, is better designed to improve the magnetic performance and enhance the stability of the MIMs.²² Thus, the magnetic adsorbents not only have strong special recognition and absorption ability of MIMs but also combine superparamagnetism and high surface area of magnetic materials.²³ Recently, some magnetic MIMs had been synthesized and reported in the literature.^{24–30}

Dicofol, as one of the major classes of the organochlorine pesticides, is used on a worldwide variety of fruit, ornamentals, and field crops. However, with its similarity of the molecular structure and biological activity to dichlorodiphenyltrichloroethane (DDT), the toxicity, capacity for endocrine disturbance, and carcinogenicity of dicofol also have a strong influence on the environment and human health by the biological accumulation effect.³¹ Presently, more and more countries are concerned about its continued use, and the residues of dicofol in grain, fruit, vegetables, and animal-derived foods are strictly limited. Therefore, it is very necessary to monitor the dicofol

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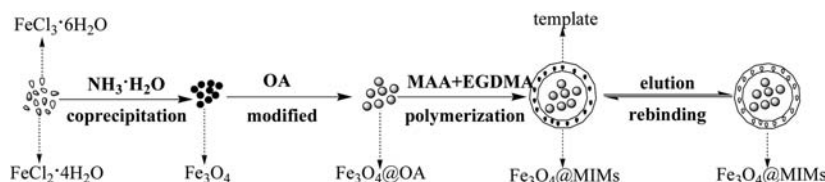


Figure 1. Fabrication procedure of Fe_3O_4 @MIMs.

residual concentration in agricultural products, which are closely related to our daily life.

Because of the complexity of the sample matrix and the trace level of dicofol in real samples, the sample pretreatment procedure is usually the most important and necessary step before instrumental analysis. Recently, some extraction methods, such as solvent extraction, always require the large amounts of solvent and multiple consequent steps, and the conventional solid-phase extraction (SPE) adsorbents (C_{18} , silica, florisil, etc.) usually lead to the co-extraction of interfering compounds because of the non-specific hydrophilic–hydrophobic interactions. Thus, the development of new adsorbents with high affinity, specific recognition, and high stability is greatly desired.

In this study, new magnetic multi-core–shell dummy MIMs (Fe_3O_4 @MIMs) via oleic acid modified were synthesized and successfully used as specific adsorbents for rapid extraction and determination of trace levels of dicofol from a complicated tea matrix. DDT was selected as the dummy template molecule because of its similar structure to dicofol and can eliminate the effect of template leaking on quantitative analysis of dicofol. In comparison to the MIMs prepared by traditional polymerization, the obtained Fe_3O_4 @MIMs adsorbent showed strong recognition ability, high binding capacity, and rapid magnetic separation behavior, which could shorten the equilibrium adsorption time with the increased extraction efficiency.

MATERIALS AND METHODS

Chemicals and Reagents. Dicofol and α -chloro-DDT were obtained from Dacheng Pesticide Co., Ltd. (Shandong, China). Methacrylic acid (MAA), polyvinylpyrrolidone (PVP), oleic acid (OA), aqueous ammonia, and 2,2-azobisisobutyronitrile (AIBN) were purchased from Kermel Chemical Co., Ltd. (Tianjin, China). Iron trichloride hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$) and iron dichloride tetrahydrate ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$) were purchased from Fuchen Chemical Co., Ltd. (Tianjin, China), and ethylene glycoldimethacrylate (EGDMA) was purchased from Sigma (St. Louis, MO). All other reagents used in the experiment were of the highest grade available. All water was double-deionized before use.

Synthesis of Fe_3O_4 @MIMs. *Preparation of Fe_3O_4 .* Fe_3O_4 was prepared by the modified co-precipitation method:³² 0.02 mol of $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ and 0.03 mol of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ were dissolved in 100 mL of deaerated water, and 2.0 mL of oleic acid was added to the mixture. With ultrasound for 20 min and stirring (600 revolutions/min) under nitrogen, 15 mL of ammonium hydroxide was added drop by drop as the temperature elevated to 60 °C. After 30 min, 2.0 mL of oleic acid was added dropwise to the mixture by stirring at 600 revolutions/min and reacted for 1 h at 80 °C. After that, the magnetic precipitates were isolated from the solvent by a permanent magnet, washed with water and ethanol in sequence, and then dried at 50 °C under vacuum for 24 h.

Preparation of Fe_3O_4 @MIMs. (a) A total of 3.0 g of PVP was dissolved in 120 mL of water by stirring at 600 revolutions/min. (b) Fe_3O_4 magnetite (4.3 mmol), DDT (2.0 mmol), and MAA (8.0 mmol) were suspended in 20 mL of toluene and then allowed to self-assemble at 4 °C for 1 h. (c) EGDMA (50 mmol) and AIBN (1.5 mmol) were dissolved in solution b and sonicated for 5 min to make it

fully dissolved. This solution was then added dropwise to solution a and then reacted at 60 °C for 24 h. (d) After polymerization, the obtained Fe_3O_4 @MIMs were separated and washed with methanol/acetic acid (9:1, v/v), water, and methanol under ultrasonic conditions. Finally, they were dried under vacuum at 50 °C for 24 h. The non-imprinted microspheres (Fe_3O_4 @NIMs) were prepared the same as above, except that the template molecule was not added.

Instrumentation and Conditions. A FTIR-8400S Fourier transform infrared (FTIR) spectrometer (Shimadzu, Japan) was employed to examine the infrared spectra of Fe_3O_4 @MIMs using a pressed KBr tablet. The morphological evaluation was carried out by KYKY-2800B scanning electron microscopy (SEM, FEL Co., USA). Magnetic properties of Fe_3O_4 @MIMs were measured with a 7307 vibration magnetometer (VSM, Lakeshore Cryotronic, Westerville, OH) at 300 K. The Fe_3O_4 @MIMs were also characterized by D8-ADVANCE X-ray diffractometer (BRUKER AXS, Germany) and TGA/SDTA851E thermogravimetric analysis (TGA, PerkinElmer Instruments Co., Ltd., Shanghai, China). The chromatographic analysis was carried out on a Shimadzu GC-2014 system, equipped with a split/splitless injector and ECD-2014 detection (Shimadzu, Japan). High-purity nitrogen (99.999%) was used as a carrier gas with a flow rate of 5.0 mL/min and a split ratio of 5.0. The capillary column used was 30 m \times 0.53 mm inner diameter, 1 μm , with material of 5% phenyl-methylpolysiloxane (Agilent, Wilmington, DE). The temperature-programmed mode was as follows: the oven temperature was set at 210 °C and held for 20 min. The temperatures of the injection port and detection were maintained at 230 and 280 °C, respectively.

Preparation of the Tea Sample. A total of 1.0 g of tea sample or spiked sample was brewed with 100 mL of boiling water and kept boiling for 10 min. Then, the infusion was filtered with 0.45 μm filter membrane and cooled to room temperature. A total of 10 mL of tea sample solution was mixed with 40 mg of Fe_3O_4 @MIMs in a 20 mL vial with a plastic cover. Then, the mixture was vortexed for 5 min to make particles contact entirely with the sample solution. A bar of magnet was placed beside the vial and held the Fe_3O_4 @MIM particles, which had already extracted the analyte. Then, water was discarded from the vial, and the remaining adsorbent was further washed with 2 mL of methanol/water (1:1, v/v) to remove interference impurities. Finally, the analyte was eluted with 4 mL of 15% ammonia–dichloromethane by vortexing for 5 min. The eluent was evaporated at 45 °C, and the residue was redissolved in 0.5 mL of *n*-hexane for further gas chromatography (GC) analysis.

Adsorption Measurement. To investigate the adsorption thermodynamic of Fe_3O_4 @MIMs, 20.0 mg of the particles was equilibrated with various concentrations (0.015–1.34 mmol/L) of dicofol, each in a 20 mL glass bottle. After 14 h, the saturated particles were separated by a magnet and the residual concentration of dicofol was determined by GC with an electronic capture detector. The dynamics method was the same as the static method, except for different times (1, 3, 5, 7, 9, 15, 20, 30, 60, and 120 min) at a constant concentration (0.038 mmol/L). The absorption quantity (Q) of dicofol was calculated by subtracting the free concentrations (C_{free}) from the initial concentrations. The same experiment was performed using the non-imprinted particles. Meanwhile, the maximum binding quantity (Q_{max}) and dissociation constant (K_D) were estimated by processing with the Scatchard equation.

$$\frac{Q}{C_{\text{free}}} = \frac{Q_{\text{max}} - Q}{K_D} \quad (1)$$

RESULTS AND DISCUSSION

Morphology and Structure of Fe_3O_4 @MIMs. The fabrication procedure of Fe_3O_4 @MIMs is schematically shown in Figure 1, and the morphology of Fe_3O_4 @MIMs observed from SEM is shown in Figure 2. As illustrated, the

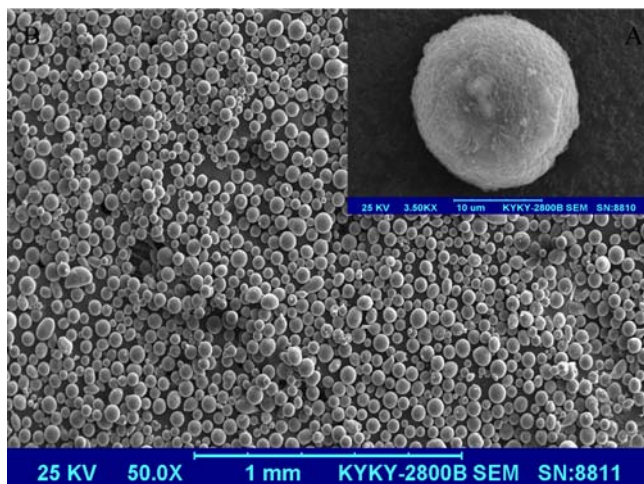


Figure 2. SEM images of Fe_3O_4 @MIMs.

shape of the particles was a roughly uniform spherical shape, which was suitable for rebinding of template molecules, and the size was commonly 7–15 μm in diameter. Fe_3O_4 @MIMs combined the characters of both molecular imprinting polymer (MIP) and magnetic nanoparticles, and their physical and chemical properties were stable.³³ The MIP shell not only made Fe_3O_4 @MIMs have biocompatibility and stability but also prevented magnetic Fe_3O_4 nanoparticles from oxidizing and aggregating. Additionally, it was also found that the micropore on the surface of NIMs was well-distributed but the average pore diameter was slightly smaller than that of MIMs, which might be ascribed to the elution of templates during the preparation of MIMs.³⁴ It revealed that the imprinted cavities could improve the mass transfer rate for rebinding and releasing the template molecules.

The FTIR spectra of Fe_3O_4 , Fe_3O_4 @oleic acid, and Fe_3O_4 @MIMs (Figure 3) indicated that the characteristic absorption

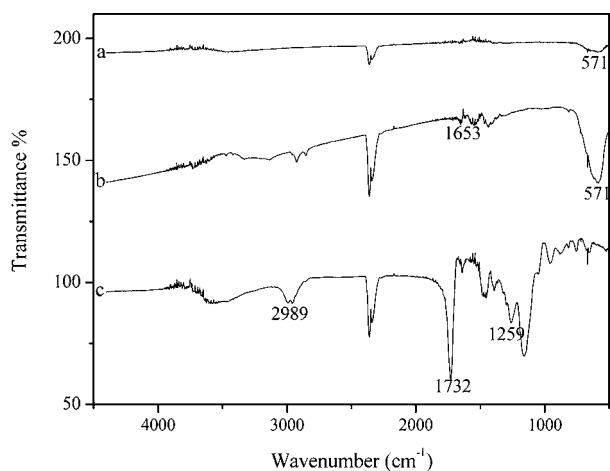


Figure 3. FTIR spectra of (a) Fe_3O_4 , (b) Fe_3O_4 @oleic acid, and (c) Fe_3O_4 @MIMs.

band of Fe–O in Fe_3O_4 was around 571 cm^{-1} (Figure 3a). The peak of 1653 cm^{-1} in Figure 3b came from the C=C group of oleic acid. In Figure 3c, we could see the peaks of the C–O group at 1259 cm^{-1} , the C=O group at 1732 cm^{-1} , and the C–H group of $-\text{CH}_2-$ and $-\text{CH}_3$ at 2989 cm^{-1} . All of this indicated that the MAA layer had been successfully formed on the surface of Fe_3O_4 @oleic acid.

The X-ray diffraction (XRD) patterns of Fe_3O_4 (curve a), Fe_3O_4 @oleic acid (curve b), and Fe_3O_4 @MIMs (curve c) were investigated also, and the results are shown in Figure 4. In the

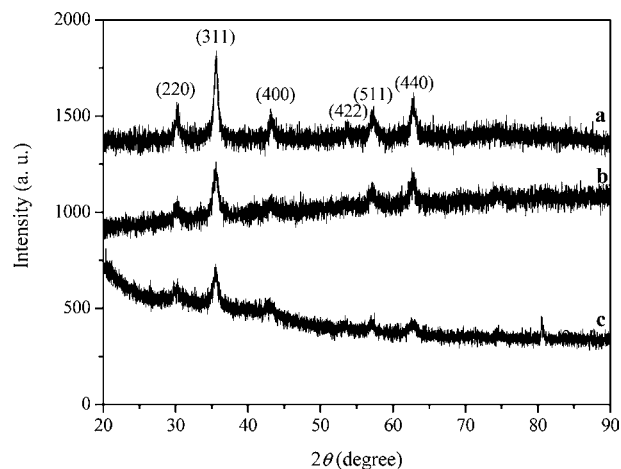


Figure 4. XRD patterns of (a) Fe_3O_4 , (b) Fe_3O_4 @oleic acid, and (c) Fe_3O_4 @MIMs.

2θ range of 20–90°, six characteristic peaks for magnetite ($2\theta = 30.19^\circ$, 35.58° , 43.35° , 53.37° , 56.95° , and 62.7°) were observed for the three samples, and the peak positions at the corresponding 2θ value were indexed as (220), (311), (400), (422), (511), and (440), which matched well with the database of magnetite in the Joint Committee on Powder Diffraction Standards (JCPDS) International Center for Diffraction Data (JCPDS Card 19-629). Moreover, the peak positions were unchanged upon coating the polymer layers and polymerization, indicating that the crystalline structure of the magnetite was essentially maintained.

Properties of Fe_3O_4 @MIMs. The magnetic property is crucial to magnetic particles for their applications in fast extraction and separation. In this work, the magnetic properties of Fe_3O_4 , Fe_3O_4 @oleic acid, and Fe_3O_4 @MIMs were investigated by VSM. Hysteresis loops in Figure 5 showed that there was no magnetic hysteresis, which indicated that both Fe_3O_4 @oleic acid and Fe_3O_4 @MIMs revealed superparamagnetic behavior. Fe_3O_4 @oleic acid had the saturation magnetization of 62.1 electromagnetic units (emu)/g, and Fe_3O_4 @MIMs exhibited the magnetic property of 56.8 emu/g. The decrease of the magnetization value was possibly attributed to the presence of additional MIM layers. The outstanding magnetic property of Fe_3O_4 @MIMs was most likely due to the following: First, the supporter core was not a single Fe_3O_4 particle but multi- Fe_3O_4 cores, which resulted in excellent superparamagnetism. Second, the supporter contained a large portion of the polymer that was used as the binder for Fe_3O_4 nanoparticles, which significantly reduced the density of the obtained Fe_3O_4 @MIMs.²¹ Furthermore, the superparamagnetism of Fe_3O_4 @MIMs prevented magnetic beads from aggregating and enabled them to respond to the magnetic

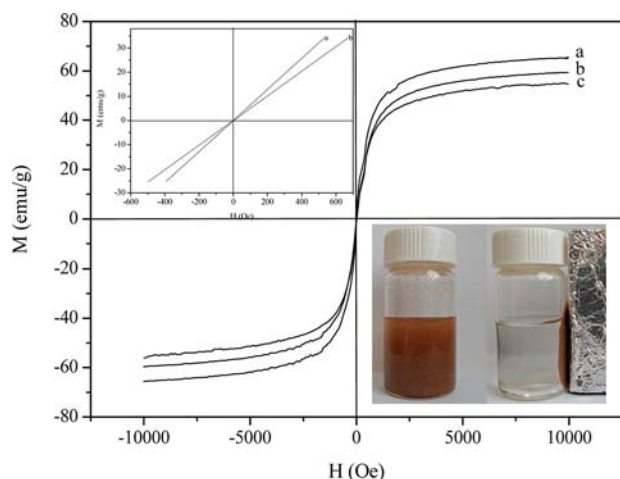


Figure 5. Hysteresis loop of (a) Fe_3O_4 , (b) Fe_3O_4 @oleic acid, and (c) Fe_3O_4 @MIMs. The inset shows the separation and redispersion processes of a solution of Fe_3O_4 @MIMs in the absence (left) and presence (right) of an external magnetic field.

field without magnetization. As illustrated in Figure 5, the rapid separation of the dispersed Fe_3O_4 @MIMs (about 15 s) from the sample solution in the presence of an external magnetic field could be easily visualized.

TGA curves of the Fe_3O_4 particles, Fe_3O_4 @oleic acid, and Fe_3O_4 @MIMs are shown in Figure 6. The initial weight loss

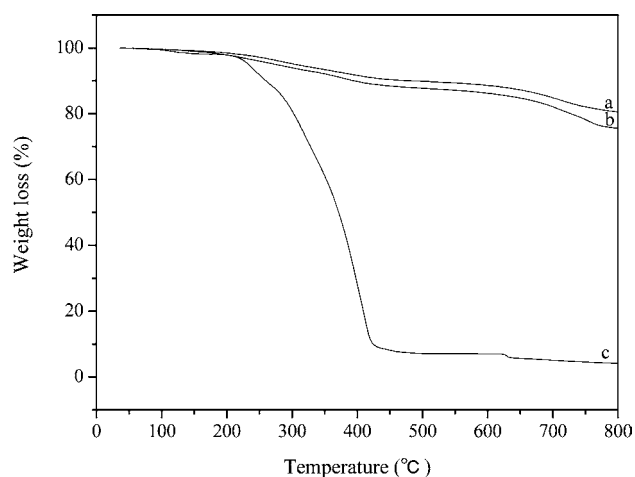


Figure 6. TGA curves of (a) Fe_3O_4 , (b) Fe_3O_4 @oleic acid, and (c) Fe_3O_4 @MIMs.

step of the three samples below 220 °C could be attributed to the elimination of the residual water or solvent in the samples. For the Fe_3O_4 particles (Figure 6b), the one-step mass loss of about 12% between 220 and 460 °C indicated that the oleic acid adsorbed on the Fe_3O_4 particles could not be fully washed out. The thermal decomposition process of the pure Fe_3O_4 particles differed from that of the Fe_3O_4 particles modified with oleic acid (Figure 6a). As seen in Figure 6c, the pronounced weight loss (about 85%) in the temperature range of 220–420 °C was caused by the thermal degradation of the MIM polymers. About 5% of the material remaining at 800 °C was Fe_3O_4 particles. The TGA analysis also revealed that the prepared Fe_3O_4 @MIMs included both inorganic and organic composites.³⁵

The binding ability of the obtained particles was analyzed in equilibrium binding experiments. On the basis of the Scatchard equation, the saturated adsorption capacity of Fe_3O_4 @MIMs was 16.0 $\mu\text{mol/g}$, 2.5 times the capacity of Fe_3O_4 @NIMs (6.4 $\mu\text{mol/g}$), which suggested that Fe_3O_4 @MIMs possessed high adsorption capacity for the removal of dicofol from an aqueous solution. Fe_3O_4 @NIMs might also bind some dicofol molecules possibly attributed to the existence of MAA, which could combine with dicofol through a hydrogen bond, while Fe_3O_4 @MIMs could recognize the target molecule because of the existence of molecularly imprinted adsorption sites with shape, fixed size, binding sites, and specific interaction between dicofol and recognition sites. The adsorption kinetic curves of dicofol showed an overall 2-fold increase in the adsorption capacity with Fe_3O_4 @MIMs versus Fe_3O_4 @NIMs. Moreover, the adsorption rate of Fe_3O_4 @MIMs increased rapidly in the first 5 min and then slightly increased thereafter until 9 min.

Analysis of Tea Samples. Six brands of tea products collected from the local markets of Baoding were pretreated and determined, and trace levels of dicofol (0.49–5.29 ng/g, which were lower than the national residue limit of China of 0.1 mg/kg) were observed in five brands of the samples (Figure 7).

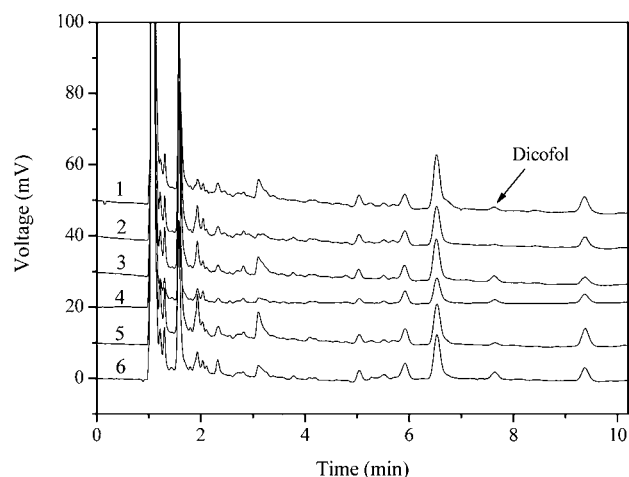


Figure 7. Chromatograms of different brands of tea products: 1, bolay tea; 2–3, green tea; and 4–6, oolong tea).

The chromatogram of the blank samples showed that there was no interference peaks at the retention time of dicofol but the peak of DDT could be observed, resulting from the template leaking of the adsorbents. As seen in Figure 8A, the peaks of the target analyte (dicofol) and dummy template (DDT) could be separated by GC analysis, thus eliminating the effect of template leakage on quantitative analysis of dicofol. Under the optimized conditions, good linearity was observed for dicofol throughout the concentration range (0.2–160 ng/g) and the limit of detection based on a signal-to-noise ratio of 3 was 0.05 ng/g. Recovery experiments were carried out by spiking three different levels of the analyte (100.0, 10.0, and 1.0 ng/g) into tea samples, and the results revealed that the average recovery of dicofol was in the range of 86.3–95.5%, with the relative standard deviation (RSD) $\leq 4.6\%$ ($n = 3$). Figure 8B revealed that Fe_3O_4 @MIMs as an adsorbent provided better purification ability than the other conventional adsorbents, such as C_{18} , Florisil, etc. Furthermore, to further evaluate the recognition properties of Fe_3O_4 @MIMs, a dicofol structural analogue named methoxychlor was also fortified into the spiked tea

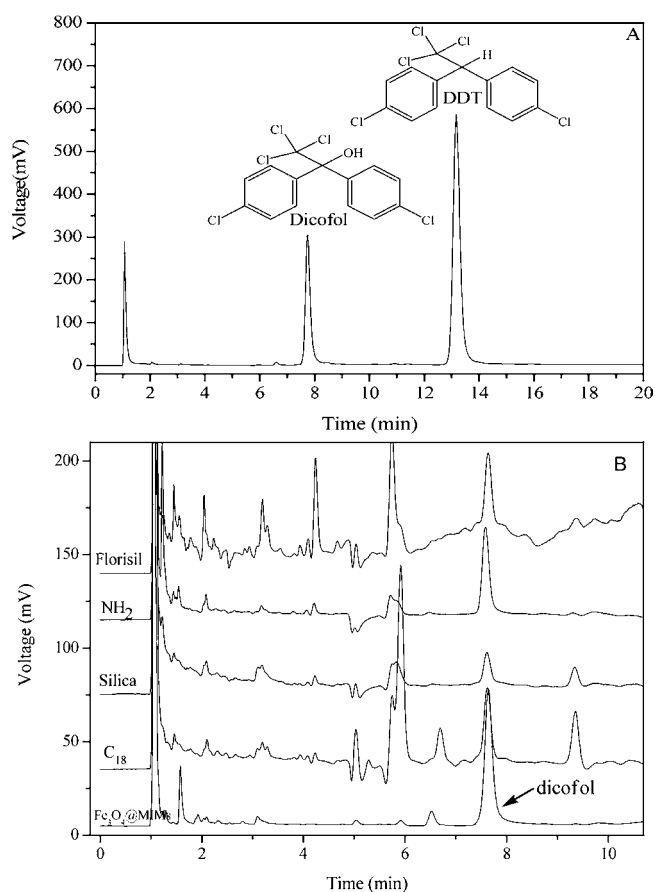


Figure 8. (A) Chromatograms of standard solution and (B) comparison of the purification effect of Fe_3O_4 @MIMs to other adsorbents.

samples and analyzed by the proposed method. The results indicated that the existence of methoxychlor had not obvious effect on the recovery of dicofol, and it could be fully separated with dicofol by the following GC analysis. The recoveries of methoxychlor at the three spiked levels ranged from 85.2 to 93.4%, which was slightly below the recovery of dicofol on Fe_3O_4 @MIMs. Meanwhile, other compounds originated from the tea matrices were significantly eliminated (Figure 8), which further demonstrated the special selectivity of Fe_3O_4 @MIMs. All of the above results indicated that Fe_3O_4 @MIMs had better special recognition ability, and it was very suitable to be exploited in a rapid isolation of the trace level of the target analyte in a complicated tea product.

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Notes

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